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1 Infant adiposity following a randomised controlled trial of a
2 behavioural intervention in obese pregnancy.

3

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49 **Runningtitle.**

50 Infant adiposity after RCT in obese pregnancy.

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81 **Abbreviations**

82 BISQ- Brief Infant Sleep Questionnaire; BMI- Body Mass Index;
83 CDM- Covariate-dependent Missing ; FFQ- Food Frequency
84 Questionnaire; GDM- Gestational Diabetes; GI- Glycaemic
85 Index; GL- Glycaemic Load; GWG- Gestational Weight Gain;
86 IPAQ- International Physical Activity Questionnaire; MET-
87 Metabolic Equivalent of Energy Expenditure; MAR- Missing at
88 Random; MNAR- Missing not at Random; UPBEAT-UK
89 Pregnancies Better Eating and Activity Trial.

90 **Contributors' Statement Page**

91 Dr Nashita Patel, Mr Paul Seed, Dr Dharmintra Pasupathy and
92 Professor Lucilla Poston conceptualized and designed the
93 study, drafted and carried out the initial analyses, critically
94 reviewed the manuscript, and approved the final manuscript
95 as submitted.

96 Dr Louise Hayes, Ms Julia Levin, Dr Sara White and Ms Angela
97 Flynn carried out the initial dietary and physical activity
98 analyses. All these authors critically reviewed and approved
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108 the final manuscript as submitted.

Abstract**Objective.**

Randomised controlled trials are required to address causality in the reported associations between maternal influences and offspring adiposity. The aim of this study was to determine whether an antenatal lifestyle intervention in obese pregnant women associated with improved maternal diet and reduced gestational weight gain leads to a reduction in infant adiposity and sustained improvements in maternal lifestyle behaviours at 6 months postpartum.

Subjects and Methods.

We conducted a planned postnatal follow up of a randomised controlled trial (UPBEAT) of a complex behavioural intervention targeting maternal diet (glycemic load and saturated fat intake) and physical activity in 1555 obese pregnant women. The main outcome measure was infant adiposity, assessed by subscapular and triceps skinfold thicknesses. Maternal diet and physical activity, indices of the familial lifestyle environment, were assessed by questionnaire.

Results.

698 (45.9%) infants (342 intervention, 356 standard antenatal care) were followed up at mean age 5.92 months. There was

131 no difference in triceps skinfold thickness z-scores between
132 the intervention vs. standard care arms (difference -0.14 SD,
133 95% CI -0.38 to 0.10, $p=0.246$), but subscapular skinfold
134 thickness z-score was 0.26 SD (-0.49 to -0.02; $p=0.03$) lower in
135 the intervention arm. Maternal dietary glycemic load (-35.34; -
136 48.0 to -22.67; $p<0.001$) and saturated fat intake (-1.93%
137 energy; -2.64 to -1.22; $p<0.001$) were reduced in the
138 intervention arm at 6 months postpartum. Causal mediation
139 analysis suggested that lower infant subscapular skinfold
140 thickness was mediated by changes in antenatal maternal diet
141 and gestational weight gain rather than postnatal diet.

142

143 **Conclusion.**

144 This study provides evidence from follow-up of a randomised
145 controlled trial that a maternal behavioural intervention in
146 obese pregnant women has the potential to reduce infant
147 adiposity and to produce a sustained improvement in
148 maternal diet at 6 months postpartum.

149

150 **Introduction**

151 The high prevalence of childhood obesity is a major health
152 concern, with 27.3% of children estimated to be overweight or
153 obese in the USA¹. A combination of antenatal and postnatal
154 exposures including environmental factors have been
155 implicated in the development of childhood obesity^{2,3}, which
156 has been shown to track into adulthood¹. Observational
157 studies suggest that manipulation of maternal metabolism
158 through diet and/or physical activity in the antenatal period
159 has the potential to reduce childhood obesity^{2,4} and this has
160 been unequivocally achieved in pregnant obese experimental
161 animals and their offspring⁵. These observations have led to a
162 consensus that obesity is in part ‘programmed’ *in-utero*, in
163 keeping with the ‘developmental programming’ hypothesis⁵.
164 Recent analyses using Mendelian randomisation methods have
165 provided evidence for a causal relationship between maternal
166 pregnancy body mass index (BMI) and glucose with birth
167 weight⁶, but any lasting causal effect on later infant adiposity
168 is unknown. Well-designed randomized controlled trials in
169 pregnant women and their offspring are required to infer
170 causality through minimising selection bias and confounding^{5,7}.

171

172 We undertook an RCT, the UK Pregnancies Better Eating and
173 Activity Trial (UPBEAT) of a dietary and physical activity
174 intervention in 1555 obese pregnant women⁸. Women were
175 randomised to standard antenatal care or standard antenatal
176 care with an intense behavioural intervention that focussed on
177 improving insulin sensitivity through reducing dietary glycaemic
178 load and saturated fat intake⁸. Although the intervention did
179 not reduce gestational diabetes (GDM) or large for gestational
180 age delivery, the primary outcomes, there were significant
181 improvements in maternal antenatal diet (maternal glycaemic
182 load/day at 28 weeks' gestation, mean difference -21, SD -26
183 to -16, $p < 0.0001$), a reduction in maternal anthropometric
184 measures of body fat assessed by sum of skinfold thicknesses
185 (-3.2mm, -5.6 to -0.8, $p = 0.008$), lower total gestational weight
186 gain (GWG) (-0.55kg, -1.08 to -0.02, $p = 0.041$), and a modest
187 improvement in physical activity at 28 weeks' gestation (295
188 min/week, 108 to 485, $p = 0.0015$)⁸, all of which have been
189 implicated in childhood obesity.

190

191 To examine the hypothesis that the lifestyle intervention
192 might reduce the influence of maternal obesity on offspring
193 adiposity, our principal aim was to assess whether the UPBEAT
194 intervention was associated with a reduction in measures of

195 childhood adiposity at 6 months of age, a pre-defined
196 hypothesis within the trial protocol⁹. We also examined
197 whether the pregnancy intervention had lasting effects on
198 maternal diet and physical activity, and on known postnatal
199 determinants of infant adiposity, including breastfeeding.

200 **Patients and Methods**

201 *Study design and setting*

202 Between July 2010 and May 2015, we conducted a planned
203 follow up at 6 months postpartum of mothers and their
204 offspring who had participated in the UPBEAT RCT in eight
205 inner-city NHS Trust Hospitals in the UK. The study design and
206 protocol⁹ were approved by the NHS Research Ethics
207 Committee (UK Integrated Research Application System;
208 reference 09/H0802/5).

209

210 *Participants and consent*

211 1555 women were recruited to the UPBEAT trial (≥ 16 years of
212 age; pre-pregnancy BMI ≥ 30 kg/m²). Exclusion criteria included
213 pre-existing disease and multiple pregnancy⁹. Following
214 informed consent for themselves and follow up of their infants
215 at 6 months postpartum, the participants were randomised to
216 the intervention or standard antenatal care at 15⁺⁰-18⁺⁶ weeks'
217 gestation. For the purposes of this follow up study, women
218 (but not their children), were excluded if pregnant at 6 months
219 postpartum. If a participant had withdrawn from the trial but
220 was willing to take part (n=2), written consent was obtained at
221 the 6 month visit. Infants were excluded if aged ≤ 4 months or

222 ≥ 8 months of age at this visit. Comparison of demographic
223 details at trial entry was made between women who declined
224 to participate and those who took part.

225

226 *Outcomes*

227 *Infant anthropometry*

228 The principal outcome of interest was infant adiposity
229 assessed by measurement of infant skinfold thicknesses
230 (triceps and subscapular, measured in triplicate by trained
231 research staff using infant skinfold callipers). Subsidiary infant
232 outcomes of infant adiposity included sum of skinfold
233 thickness (calculated by addition), estimated total body fat
234 (calculated by applying validated equations specific for infant
235 sex¹⁰), weight (using a calibrated scale⁹), abdominal and upper
236 mid-arm circumferences. For these measures, when reference
237 World Health Organization population data were available, z-
238 scores were calculated¹¹, including adjustment for infant age,
239 sex and length. These standards are applicable to infant
240 growth regardless of ethnicity, socioeconomic status and
241 mode of feeding¹¹. Z-scores were calculated for infant
242 subscapular, triceps skinfold thickness, weight, BMI and arm
243 circumference but not for sum of skinfold thicknesses.
244 Occipitofrontal circumference, and crown-rump length and

245 crown-heel length obtained with a calibrated infantometer,
246 were also measured.

247

248 Duration of breastfeeding, weaning history, measures of
249 appetite, infant sleeping patterns, physical activity, healthcare
250 resource use and childcare⁹ were pre-specified outcomes.
251 These were evaluated using the Infant Feeding and Growth
252 Questionnaire¹², the Child Eating and Behaviour
253 Questionnaire¹³, the BISQ (Brief Infant Sleep Questionnaire)¹⁴,
254 the Infant Behaviour Questionnaire (for child physical
255 activity)¹⁵ and questionnaires ascertaining infant health,
256 medical resource use and early care and education,
257 respectively.

258

259 Maternal dietary and physical activity analysis

260 Maternal diet at 6 months postpartum was assessed using the
261 same semi-quantitative food frequency questionnaire (FFQ)
262 and analysed as previously reported for the mothers during
263 their pregnancy⁸. Data was analysed only in questionnaires
264 which were fully completed for both maternal diet and
265 physical activity. Those with incomplete/missing dietary data
266 were excluded (65.8%). There was no missing physical activity

267 data. The main outcomes of interest were maternal dietary
268 glycaemic load, saturated fat intake and energy intake. Other
269 outcomes included glycaemic index (GI), glycaemic load (GL),
270 protein and fibre intake. Physical Activity was assessed, as it
271 had been in pregnancy, using the International Physical
272 Activity Questionnaire (IPAQ) and summarised as metabolic
273 equivalents (METs) of energy expenditure¹⁶.

274

275 *Statistical analyses*

276 A complete-case analysis was undertaken for all participating
277 mothers and infants. Treatment effects for continuous
278 outcomes were expressed as differences in means obtained
279 from multivariable linear regression, and binary endpoints as
280 risk ratios with 95% confidence intervals (95%CI) obtained
281 using binomial regression. For both we adjusted for
282 minimisation variables (maternal BMI at trial enrolment, parity
283 and ethnicity) and infant sex and age at follow up. We
284 evaluated the number of intervention contact sessions during
285 pregnancy on measures of infant adiposity.

286 Although loss to follow-up was similar in both of the trial arms,
287 we assessed the possibility that loss to follow-up resulted in
288 selection bias using three complementary methods (further
289 details in Supplementary Text 1). All sets of analyses were pre-

290 planned sensitivity analyses. First, we used Little's chi-squared
291 covariate-dependent missing (CDM) test to explore evidence
292 of data being missing not at random (MNAR), i.e. examining
293 the possibility that in those who were lost to follow-up the
294 effect of the intervention on outcomes differed from those
295 who did attend the follow-up¹⁷. This was done for both
296 offspring and maternal outcomes. Second, for the primary
297 offspring outcomes only (subscapular and triceps skinfold
298 thicknesses), we generated several simulation datasets, over a
299 range of scenarios regarding missing data in both arms of the
300 study that were informed by predictors of loss to follow-up
301 (maternal BMI, parity and ethnicity)¹⁸. The scenarios selected
302 aimed to cover a range of plausible situations that could result
303 in bias under the assumption of data being missing at random
304 (MAR). Thirdly, for the primary infant outcomes we used
305 multivariate imputation chained equations to impute missing
306 data for infant adiposity. Data were imputed to create 50
307 datasets using 10 burn-in iterations for live-born infants using
308 the following in the multivariate equations: maternal trial
309 entry BMI, age, ethnicity, parity, early pregnancy smoking
310 status, randomisation allocation, measures of maternal
311 anthropometry including GWG, maternal diet and physical
312 activity at 27-28⁺⁶, 34⁺⁰-36⁺⁰ weeks' and 6 months postpartum
313 (glycaemic load, glycaemic index, saturated fat, carbohydrate,

314 protein, energy intake), gestation at delivery, infant sex, age at
315 follow up, mode and duration of early feeding, sleep, child
316 health and infant inpatient admissions. The multivariate
317 imputations assume MAR and can also increase statistical
318 power and so allow us to explore whether loss to follow-up
319 might have resulted in type-2 statistical errors. Full details of
320 all of these sensitivity analyses are provided in Supplementary
321 Text 1. Analyses were performed using Stata version 14.0.

322 **Results**

323 *Participants*

324 Of the 1555 participants randomised to UPBEAT at 15⁺⁰-18⁺⁶
325 week's gestation between July 2010 and May 2015 and with a
326 live born infant, 1522 were approached at this time. Of these
327 1522, 720 (47.3%) infants and 707 (46.5%) mothers took part in
328 this study. Thirteen mothers were excluded as they were
329 pregnant at time of study, and 22 infants were excluded
330 because the follow up appointment was held ≤ 4 months or ≥ 8
331 months postpartum (Figure 1). In comparison to those who did
332 not take part, mothers who attended the 6 month visit were on
333 average 1.3 years older, more likely to be Caucasian,
334 nulliparous, to have had GDM in the index pregnancy (28.2%
335 vs. 23.3%; $p=0.041$), and were less likely to be current smokers
336 (Supplementary Table 1a, Supplementary Text 1). There were
337 no differences in maternal early pregnancy BMI and sum of
338 skinfold thicknesses between women who participated in the
339 6 month follow-up visit compared to those who did not.

340 Women in the intervention arm demonstrated reduced GWG
341 as previously reported⁸. The infants who attended the 6
342 month appointment had a longer gestational age at delivery
343 (by 2 days), were 67g heavier, and more likely to have been

344 breastfed at birth than those that did not attend

345 (Supplementary Table 1b).

346

347 There was no difference between mean maternal BMI

348 between the intervention and standard care groups at trial

349 entry (36.17 vs. 36.31 kg/m², respectively) or at 6 months

350 postpartum (36.26 vs. 36.45 kg/m², respectively). The

351 incidence of maternal smoking at 15⁺⁰-18⁺⁶ weeks' gestation

352 was higher in the standard antenatal care arm in comparison

353 to the intervention arm (5.6% vs. 2.0%)(Table 1). There were

354 no differences in all other demographic and clinical variables

355 between the two study arms (Table 1).

356

357 *Infant anthropometry*

358 Three hundred and fifty six infants in the standard antenatal

359 care arm and 342 infants in the intervention arm (mean age

360 5.82 months) had anthropometric measurements at age 6

361 months. There was no statistical difference in triceps skinfold

362 thickness in the intervention vs. the standard care arm

363 (difference -0.14 SD, 95% CI -0.38 to 0.10), p=0.246), but

364 subscapular skinfold thickness z-score was -0.26 SD (-0.49 to -

365 0.02; p=0.031) lower in the intervention arm (Table 2). Infants

366 in the intervention arm had a 5% lower subscapular skinfold
367 thickness (-0.38mm; -0.70 to -0.06; $p=0.021$), compared to
368 infants in the standard antenatal care arm (Table 2). The infant
369 sum of skinfold thickness was 0.63mm lower in the
370 intervention arm, but did not reach statistical significance
371 ($p=0.058$) in comparison to the standard antenatal care arm
372 (Table 2). There were no differences in BMI z-score and
373 abdominal circumference (Table 2) or in other anthropometric
374 measures between the two arms (Supplementary Table 2).

375 Maternal smoking status at trial entry did not influence the
376 difference in subscapular skinfold thickness between the two
377 arms (Supplementary Table 3). Undertaking sensitivity
378 analyses for deviation from the missing at random assumption,
379 significant differences in infant subscapular skinfold thickness
380 (mm) were found within a range of -0.35 to -0.38mm
381 dependent on the assumption of missingness taken
382 (Supplementary Text 1 and Supplementary Table 4). Similar
383 results to the complete-case analysis were also observed for
384 infant triceps skinfold thickness (Supplementary Table 5).

385

386 There was no difference in infant feeding between the two
387 trial arms, nor appetite and satiety responsiveness and infant
388 childcare. Infants were exclusively breastfed, on average for

389 82.7 (SD 65.3) days and total number of hours spent sleeping
390 were similar between arms (Supplementary Table 7). There
391 was an increase in infant inpatient nights in the intervention
392 arm, attributable to 1 infant requiring long-term hospital
393 admission due a ventricular septal defect repair
394 (Supplementary Table 7). We observed no differences in infant
395 use of medications (Supplementary Table 6) or in cause of
396 hospital inpatient admissions, except for gastrointestinal
397 related disorders, which were lower in the intervention arm
398 (Supplementary Table 8). There was no association between
399 the number of antenatal contact sessions with the health
400 trainer and measures of infant anthropometry (Supplementary
401 Table 9).

402 No interactions were observed between randomisation
403 allocation and infant sex (Supplementary Table 10), but there
404 was a significant interaction of breast feeding (< 3mths/
405 ≥ 3 mths) with the intervention; triceps skin fold thickness was
406 lower in infants of mothers in the intervention arm who
407 breastfed ≥ 3 months vs those in the standard care arm -
408 0.90mm (-1.59 to -0.21); $p=0.011$; Wald interaction test;
409 $p=0.016$) (Figure 3). Similar patterns of differences of effect by
410 breastfeeding for sum of skinfold thicknesses, estimated total
411 body fat and arm circumference did not achieve statistical

412 significance (p-values for interactions all ≥ 0.05)

413 (Supplementary Table 11).

414

415 *Maternal diet and physical activity*

416 In those women who provided complete dietary data GI, GL,

417 saturated fat and total energy intake were reduced in the

418 mothers in the intervention arm in comparison to standard

419 care, as well as a significant reduction in total fat and protein

420 intakes (Figure 2 & Table 3). When the under-reporters

421 (calorie intake) were included in sensitivity analyses, there

422 were no differences in the effect size estimates of dietary

423 variables. Furthermore we found no difference in maternal

424 characteristics (including maternal age, BMI and

425 socioeconomic deprivation status) between those under-

426 reporting and those not under-reporting calorie intake. There

427 was no effect of the intervention on maternal physical activity

428 (Table 3).

429

430 Causal analysis suggested direct effects of the intervention

431 associated reduction in maternal early GWG (between 15-18⁺⁶

432 and 27-28⁺⁶ weeks' gestation) ($p=0.015$), late GWG (between

433 27-28⁺⁶ and 34-36 weeks' gestation) ($p=0.009$), total GWG

434 (p=0.014) and maternal dietary saturated fat intake at 27-28⁺⁶
435 week's gestation (p=0.016) in relation to infant subscapular
436 skinfold thickness at age 6 months (Supplementary Figure 1).
437 In contrast, there was no suggested effect of postnatal
438 maternal diet on the observed differences in infant
439 subscapular skinfold measurements (Supplementary Figure 2).
440 As there was no effect of the intervention on maternal
441 physical activity, there was no rationale for exploring a causal
442 mediating impact of maternal physical activity on offspring
443 adiposity.

444

Discussion

This study has addressed the effect of a pregnancy lifestyle behavioural intervention in obese women on offspring adiposity and maternal diet and physical activity at 6 months postpartum. We have found, to our knowledge for the first time, that a dietary and physical activity intervention in pregnant women with obesity was associated with a reduction in a measure of offspring adiposity, and that changes in maternal diet during pregnancy persisted into the postnatal period. Further analyses suggested that the effect of the intervention on offspring adiposity was independently mediated by the observed reduction in maternal gestational weight gain, dietary fat and energy intake in pregnancy and therefore an expectation that lifestyle interventions have the potential to reduce offspring adiposity. Subscapular skinfold thickness, in comparison to the other anthropometric measurements assessed, is recognised as an accurate index of central adiposity, with a generally lower measurement error than triceps skinfold thickness^{19,20}. In children and adults, subscapular skinfold thickness has been related to impaired glucose metabolism, and in adolescents to increased serum cholesterol concentration^{21, 22}. It is plausible, therefore that the maternal dietary and weight changes resulting from the

468 intervention may influence infant body composition towards a
469 healthier metabolic profile²²⁻²⁴.

470

471 Although the magnitude of difference in this measure of
472 adiposity (subscapular skinfold thickness) between
473 intervention and controls arms was modest (5%), it reflected a
474 0.26 reduction in z-score, which incorporated adjustment for
475 infant sex, age and length to allow comparisons to a reference
476 population. Indications from mother-child cohorts, including
477 the USA Project Viva study, suggest that even modest
478 differences in body composition at age 6 months may be
479 amplified as the child grows older, and that this may be
480 apparent as early as 3 years²⁵. The Bogalusa Heart Study
481 observed that greater offspring childhood subscapular skinfold
482 thickness related to parental type 2 diabetes was associated
483 with a subsequent adverse metabolic profile in early
484 adulthood²². Any persistent influence of the intervention on
485 childhood obesity will only be revealed as the children grow
486 up, but an abundance of evidence suggests that increased
487 adiposity tracks from infancy, through childhood to
488 adulthood¹.

489

490 We are aware of only two relevant similar studies. The first,
491 the Lifestyle in Pregnancy study (LIP)²⁶, assessed body
492 composition in older infants (2.8 years) of obese
493 mothers(n=157) who had been randomised to an antenatal
494 lifestyle intervention with the primary aim of reducing
495 gestational weight gain. No change in infant total fat mass, as
496 assessed by DEXA scan, was observed²⁷. However, it was not
497 reported whether this intervention modified specific
498 components of maternal antenatal diet or body composition,
499 although a reduction in median gestational weight gain was
500 observed. Secondly, a recent RCT of a low glycaemic diet, but
501 in women of heterogenous BMI, despite a difference in
502 reduction of thigh circumference found no difference in infant
503 body composition at 6 months of age between intervention
504 and control arms^{28, 29}. The difference between these studies
505 and UPBEAT may relate to the greater intensity of the UPBEAT
506 intervention, involving 8 contact sessions with health trainers,
507 at weekly intervals⁸.

508

509 There remains a paucity of data regarding the long-term
510 efficacy of lifestyle interventions in obese pregnant women⁵.
511 Our study has shown that dietary advice focussing on
512 reduction of maternal insulin resistance, as a component of a

513 complex intervention, can have a prolonged effect which may
514 have potential to improve long term health as well as familial
515 nutritional environment^{12, 30, 31}. We did not, however, find any
516 differences between groups in maternal BMI or measures of
517 adiposity at 6 months postpartum. A sustained effect of any
518 maternal dietary intervention on maternal dietary intake
519 postpartum has to our knowledge not been reported
520 previously. In contrast, in the LIMIT trial, follow up of 50.5% of
521 participants, reported no difference in maternal dietary
522 composition at 4 months postpartum³², also by self-report.
523 The lower magnitude of intervention effects on maternal
524 dietary variables compared with UPBEAT may explain these
525 differences.

526

527 Using the method of causal mediation analysis, we found
528 evidence that the lower dietary saturated fat and energy
529 intake at 28 weeks' gestation induced by the UPBEAT
530 intervention, rather than the change in glycemic load, was
531 associated with the reduction in infant subscapular skinfold
532 thickness at 6 months of age. The reduction in gestational
533 weight gain irrespective of timing and total gestational weight
534 gain were also directly associated with the observed
535 difference. These observations would concur with several

536 reports describing associations between maternal gestational
537 weight gain or diet and offspring adiposity^{4, 33, 34}. Antenatal
538 interventions shown to improve maternal diet and
539 subsequently reduce GWG may therefore be pragmatic and
540 effective measures to reduce early infant adiposity.

541

542 The observation that exclusive breastfeeding for more than 3
543 months may interact with the maternal intervention to reduce
544 offspring triceps skinfold thickness provides some evidence
545 that breast feeding may compound the benefits of the
546 maternal intervention, although caution should be exercised in
547 over-interpretation as the study was not powered to test
548 interactions such as these. The role of other intrauterine
549 exposures remains to be elucidated; whilst we previously
550 reported no differences in fasting lipids, c-peptide and insulin
551 at 28 weeks' gestation between randomisation arms⁸, ongoing
552 biochemical and metabolomic analyses in maternal and cord
553 blood may provide insight into mechanistic pathways.

554

555 A limitation of our study was the follow up of only 47.3% of
556 those infants eligible from the original RCT⁸, but this was
557 similar to the rate of follow up of recently published RCTs in
558 pregnant women^{27, 28, 35}. Due to the stringent inclusion of only

complete dietary questionnaires, maternal dietary data was calculated only for 34.2% of the mothers. The dietary data was by self report but compared favourably to a more rigorous method (triple pass 24hr recall) as assessed in the pilot trial³⁶. Strengths of the study include the prospective collection of in-depth data addressing familial and individual determinants of infant adiposity, and of maternal *in-utero* exposures. The richness of data in the UPBEAT study can be considered both a strength and limitation. Whilst providing comprehensive information relevant to developmental origins of early infant obesity, and assessment of mediation effects, limits are imposed on interpretation of secondary analyses in the context of multiple testing.

572

In conclusion, this study provides evidence of the potential for targeted intervention in obese women to improve health for the mother and her offspring. Pregnancy, as demonstrated in this study, appears to be a pragmatic 'teachable' moment for initiating long-term healthier dietary behaviours in the mother and reducing a physiologically relevant measure of adiposity in the offspring.

580

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586

587 Conflict of interests

588 All authors have no financial relationships relevant to this
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591 Supplementary information is available at the International
592 Journal of Obesity's website.

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788 Figure Legends

789 **Figure 1.**Consort diagram of participants enrolled in the UPBEAT
790 trial at 6 months postpartum

791 **Figure 2.**Maternal Glycaemic load (a), Saturated fat (b) and Energy
792 intake (c) at 6 months postpartum by randomisation allocation.

793 Abbreviations: %E- Percentage energy; kcal/day- kilocalorie per day.

794 Arithmetic mean with standard error plotted at each gestation (weeks),
795 showing nutritional consumption per day.

796

797 **Figure 3. Relationship between duration of exclusive breast**
798 **feeding and anthropometry measured at 6 months postpartum in**
799 **698 infants from the UPBEAT trial.**

800 Effect estimates/ mean differences plotted with 95% confidence intervals.

801 For triceps skinfold thickness (n=627), sum of skinfold thickness (n=547),
802 total body fat (n=547) and upper mid-arm circumference (n=676).

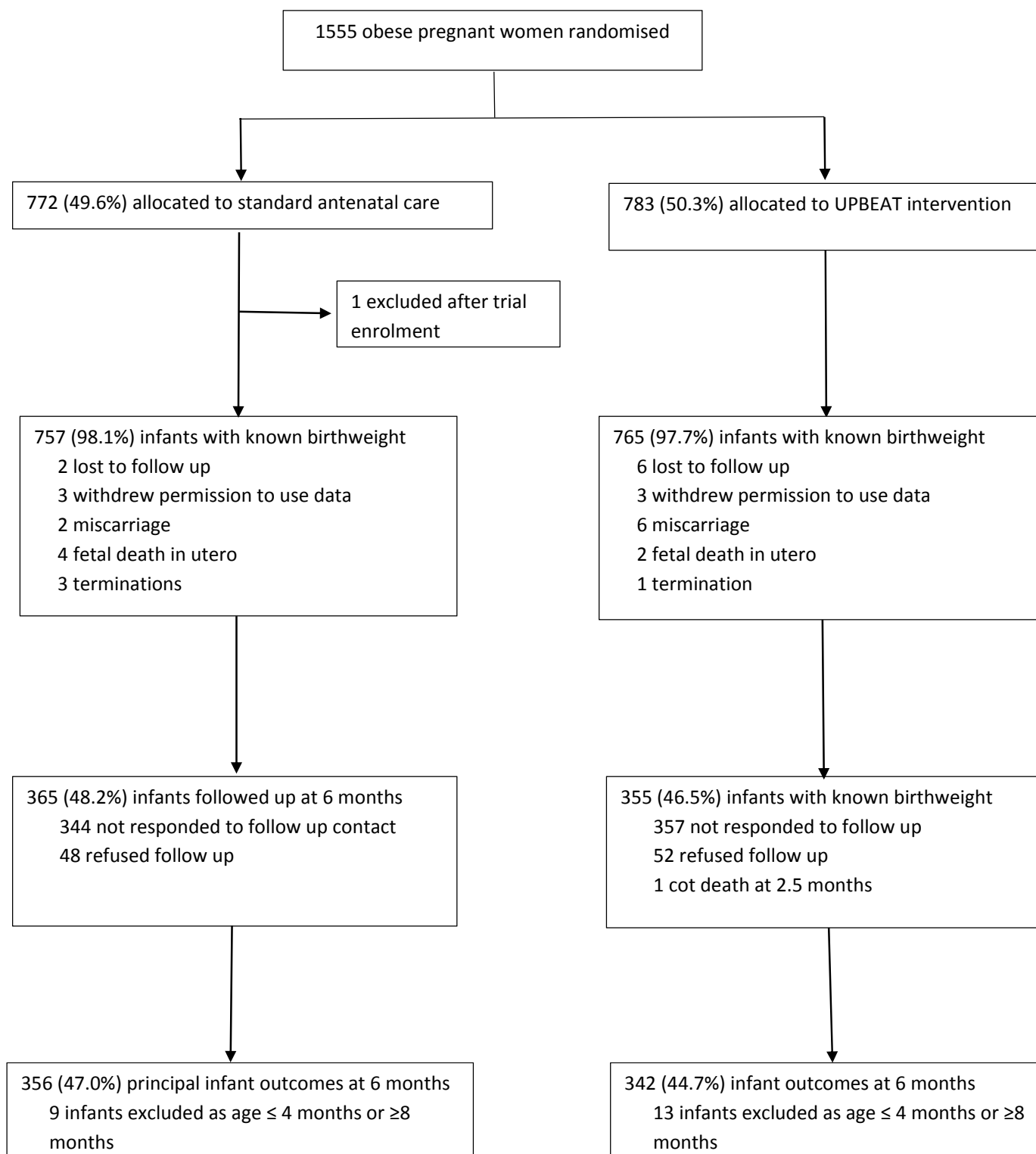
803 *Significant Wald test for interaction $p < 0.05$

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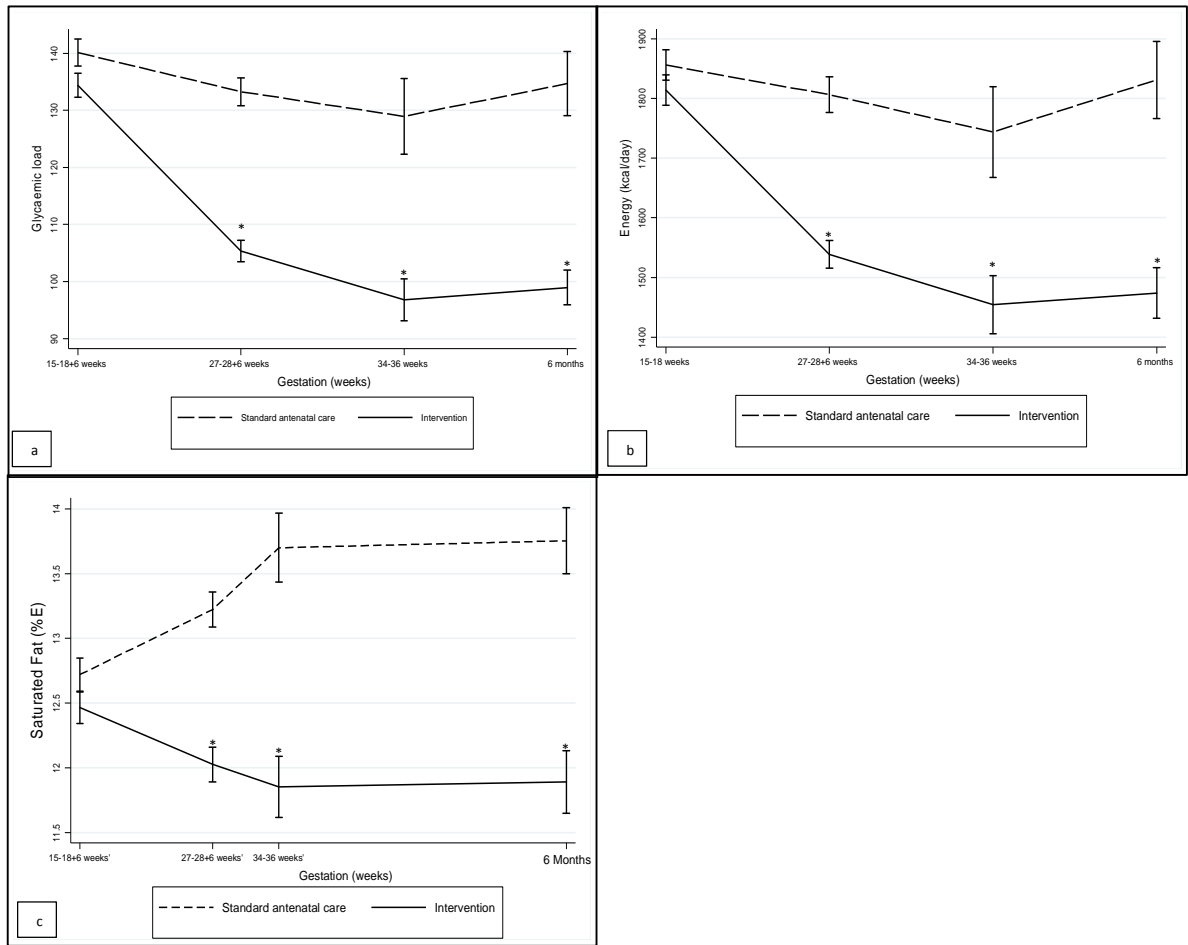
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Figure 1.



Consort diagram of participants enrolled in the UPBEAT trial at 6 months postpartum

Figure 2.

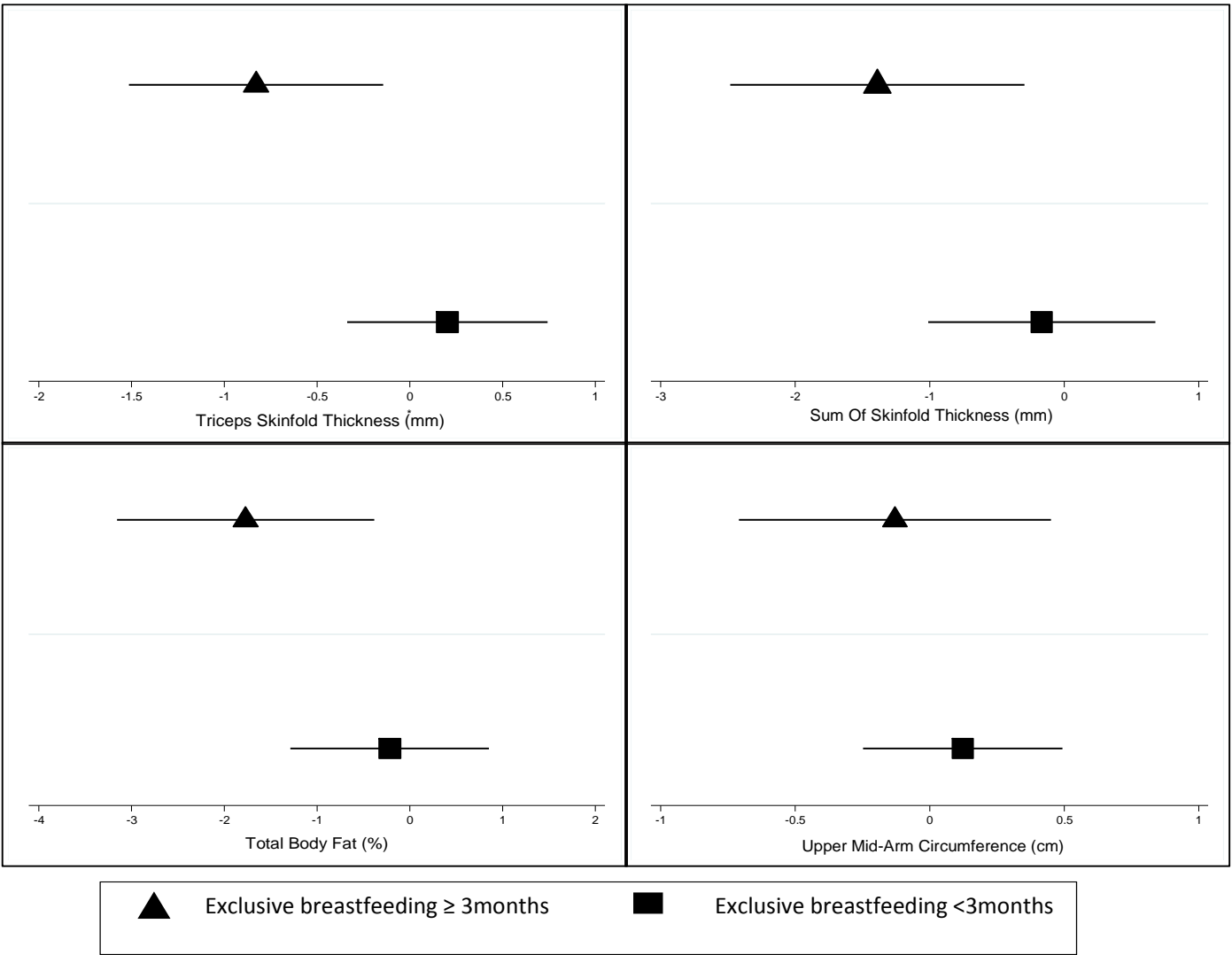


Maternal Glycaemic load (a), Saturated fat (b) and Energy intake (c) at 6 months postpartum by randomisation allocation.

Abbreviations: %E- Percentage energy; kcal/day- kilocalorie per day

Arithmetic mean with standard error plotted at each gestation (weeks), showing nutritional consumption per day. *p<0.01.

Figure 3.



Relationship between duration of exclusive breast feeding and anthropometry measured at 6 months postpartum in 698 infants from the UPBEAT trial.

For triceps skinfold thickness (n=627), sum of skinfold thickness (n=547), Total body fat (n=547) and upper mid-arm circumference (n=676).

*Significant Wald test for interaction $p < 0.05$

Table 1.

			Intervention (n=342)		Control (n= 356)
			Mean (SD)/N(%)		Mean (SD)/N(%)
Maternal demographics					
Pre-pregnancy					
Maternal age (years)		N=342	31.30 (5.04)	N=356	31.00 (5.58)
Maternal ethnicity	Asian	N=342	14 (4.1)	N=356	11 (3.1)
	Black		62 (18.1)		72 (20.2)
	Other		19 (5.6)		22 (6.2)
	White		247 (72.2)		251 (70.5)
Multiparous		N=342	169 (49.4)	N=356	174 (48.9)
Index of multiple deprivation quintiles*	1 (least deprived)	N=341	15 (4.4)	N=355	19 (5.4)
	2		29 (8.5)		19 (5.4)
	3		35 (10.3)		38 (10.7)
	4		119 (34.9)		136 (38.3)
	5 (most deprived)		143 (41.9)		143 (40.3)
Family history	GDM	N=333	10 (3.0)	N=344	11 (3.2)
	PET	N=333	40 (12.0)	N=344	33 (9.6)
	T2DM	N=341	86 (25.2)	N=356	70 (19.7)
15-18 weeks' gestation					
Current smoker [^]		N=342	7 (2.0)	N=356	20 (5.6)
Maternal anthropometry	Maternal BMI (kg/m ²)	N=342	36.17 (4.98)	N=356	36.31 (4.69)
	Systolic blood pressure (mmHg)	N=340	117.90 (11.15)	N=352	119.32 (11.00)
	Sum of skin folds (cm) [‡]	N=337	124.34 (28.46)	N=354	122.18 (25.06)
Maternal Antenatal and postpartum history					
Gestational diabetes **		N=336	97 (28.9)	N=346	93 (26.9)
Pre-eclampsia [∞]		N=340	11 (3.2)	N=353	11 (3.1)
Total gestational weight gain from pre-pregnancy weight [¶]		N=320	6.92 (4.65)	N=332	7.83 (4.41)
Maternal 6 month postpartum BMI (kg/m ²)		N=345	36.26 (5.14)	N=355	36.45 (5.41)
Change in maternal weight from 15-18 weeks to 6 months postpartum (kg)		N=344	-0.37 (7.41)	N=355	0.36 (6.71)
Infant demographics					
Infant age at 6 months follow up (months)		N=342	5.80 (0.65)	N=356	5.85 (0.72)
Gestation at birth (weeks)		N=342	39.73 (1.54)	N=356	39.55 (2.29)
Birthweight (gm)		N=342	3479.23 (529.40)	N=356	3436.55 (604.09)
Large for Gestational Age >90 th (customised) [†]		N=342	30 (8.8)	N=356	27 (7.6)
Neonatal feeding history at 72 hrs	Artificial feeding	N=341	63 (18.5)	N=354	78 (22.0)
	Breast feeding	N=341	213 (62.5)	N=354	216 (61.0)
	Partially breastfeeding	N=341	65 (19.1)	N=354	132 (37.1)

Maternal and Infant demographics by randomisation allocation at 6 month postpartum visit.

[^] Maternal current smoking at 15-18 weeks' gestation significantly different between intervention and control groups (p=0.02). *IMD quintiles are calculated for the region of residence, by fifths of the population. UK wide-scores were developed by reconciling Scottish data to English norms. ** Gestational diabetes diagnosis by International Association of Diabetes in Pregnancy Study Group criteria at 27⁺⁰ to 28⁺⁶ weeks' gestation.

‡ Calculated by the addition of biceps, triceps, suprailiac and subscapular skinfold measurements each measured in triplicate. ∞ Pre-eclampsia defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or both, on at least two occasions 4 hours apart, with proteinuria ≥ 300 mg/ 24 hours. ¶ Gestational weight gain calculated using estimated weight before pregnancy according to the Institute of Medicine Weight Management in Pregnancy Guidelines. † Customised birthweight centile calculated adjusting for maternal height and weight, ethnic origin, parity and sex of the infant.

	Intervention		Control		Mean Diff/ Risk Ratio* (95% CI)	p-value
		Mean (SD)		Mean (SD)		
Subscapular skinfold thickness z-scores**	N=267	0.08 (1.37)	N=280	0.36 (1.37)	-0.26 (-0.49 to -0.02)	0.031
Subscapular skinfold thickness (mm)	N=267	7.55 (1.86)	N=281	7.95 (2.03)	-0.38 (-0.70 to -0.06)	0.021
Triceps skinfold thickness z-scores**	N=296	0.10 (1.56)	N=298	0.24 (1.43)	-0.14 (-0.38 to 0.10)	0.246
Triceps skinfold thickness (mm)∞	N=307	9.69 (2.76)	N=320	9.87 (2.69)	-0.22 (-0.64 to 0.20)	0.305
Sum of skinfolds (mm)	N=267	17.08 (3.93)	N=280	17.71 (3.97)	-0.63 (-1.30 to 0.04)	0.058
BMI for age z-scores**	N=317	-0.07 (1.86)	N=320	0.04 (1.78)	-0.12 (-0.40 to 0.16)	0.393
Abdominal circumference (cm)	N=329	43.74 (4.73)	N=347	43.72 (6.27)	0.07 (-0.78 to 0.92)	0.872

Table 2.

Infant anthropometry by randomisation allocation at 6 months postpartum visit

*Treatment effect adjusted for minimisation variables of randomisation (maternal BMI, ethnicity and parity), infant age at 6 month follow up and infant sex. **Z-scores calculated using WHO Anthro; version 3.2.2.

Table 3.

		Intervention		Standard care		Treatment effect*	P-value	
						Mean Difference (95% CI)		
Maternal diet**								
Glycaemic Load per day	N=116	98.94 (32.80)	N=126	134.69 (62.68)		-35.34 (-48.00 to -22.67)	<0.001	
Saturated fat (%E)	N=116	11.89 (2.61)	N=126	13.75 (2.85)		-1.93 (-2.64 to -1.22)	<0.001	
Total energy (kcal/day)	N=116	1473.84 (596.60)	N=126	1831.21 (727.65)		-354.52 (-505.95 to -203.10)	<0.001	
Glycaemic Index (0-100)	N=116	53.06 (4.06)	N=126	57.04 (3.74)		-3.94 (-4.93 to -2.94)	<0.001	
Carbohydrate (%E)	N=116	47.69 (6.71)	N=126	48.03 (6.22)		-0.18 (-1.84 to 1.49)	0.835	
Total fat (%E)	N=116	29.70 (4.94)	N=126	32.26 (4.75)		-2.65 (-3.91 to -1.38)	<0.001	
Protein (%E)	N=116	22.57 (4.42)	N=126	19.82 (3.94)		2.70 (1.63 to 3.77)	<0.001	
Fibre (g/day)	N=116	12.12 (4.36)	N=126	12.27 (6.81)		-0.12 (-1.57 to 1.33)	0.873	
Maternal physical activity^		Median (IQR)		Median (IQR)		Median regression (95% CI)		
MET (min/week)†	N=349	2190 (1053, 4158)		N=358	2012 (990, 4088)		93.95 (-264.81 to 452.72)	0.607
MVPA (min/week)	N=349	120 (0, 360)		N=358	120 (0, 360)		10.43 (-39.31 to 60.18)	0.681
Walking (min/week)	N=349	420 (180, 840)		N=358	420 (180, 630)		0.00 (-68.88 to 68.88)	1.00

Maternal dietary and physical activity data by randomisation allocation at 6 months postpartum

Abbreviations: CI- Confidence Intervals; %E- %Energy; g/day- grams per day; kcal/day- kilocalories per day; MET- Metabolic equivalent of task; MVPA- Moderate and Vigorous physical activity.

*Treatment effect adjusted for maternal trial entry BMI, parity and ethnicity. ** Maternal diet- Women with a reported energy ≤ 4.5 MJ/day or ≥ 20 MJ/day at 15⁺⁰ -18⁺⁶ weeks' gestation were excluded from the analyses of diet. Dietary intervention estimates were calculated using multiple regression and adjusted for maternal pre-pregnancy current smoking status. ^ Physical activity estimates were calculated using bootstrapped (1000 replications), median regression adjusting for maternal pre-pregnancy current smoking status. † MET is defined as the energy expenditure ratio of activity to rest; one MET is approximately equal to an individual's resting energy expenditure.

